October 4, 1966

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Dear Doctor Strong:

Mr. Hoyt has turned over to me the abstract you prepared for the American Heart Association meeting in New York on October 20th. It has been read with great interest. Indeed we have been awaiting the results of this long-term study rather impatiently in the expectation that they would considerably influence the future direction and emphasis in our research program. This promises to be the case.

If you had found a definite lack of correlation between cigarette smoking and the degree of atherosclerosis, some rather definite conclusions might have been warranted. We could have assumed, rather definitely, that neither chronic nicotine absorption at customary levels, nor the absorption of any other cigarette smoke ingredient significantly influences the atherosclerotic processes, and could virtually have written this off as a possibility. We could then have focussed our attention chiefly upon the still-obscure mechanisms that precipitate acute clinical events such as thrombosis and/or infarction in subjects who have developed a predisposing degree of sclerosis. An informal conference on this latter subject was held in our offices on June 10, 1966, attended by about a dozen specialists. They seemed to agree that though atherosclerosis tends in general to predispose to infarction, yet the latter frequently occurs where there is relatively little atherosclerosis and often fails to occur where such lesions are very advanced. An effort was made to devise some experimental approaches to this problem, in the expectation that our main future interest in cardiovascular disease would lie in this area.

We had rather expected that you would find such a lack of correlation. The reasons for this expectation were as follows:

1. Our own animal studies involving superposition of chronic nicotine dosage upon an atherogenic diet showed no consistent differences between the animals receiving the alkaloid and those on the diet alone.

2. The similar post-mortem pathology studies of Wilens and Plair and of Spain, which showed little association.

3. The Framingham-Albany studies showing that smokers develop angina pectoris no oftener or earlier than non-smokers.

Jack P. Strong, M.D.

4. The fact that cigar and pipe smokers experience little greater mortality from ischemic heart diseases than non-smokers although they probably absorb as much nicotine as cigarette smokers. (This remains to be demonstrated definitely).

My reasoning throughout the course of your study has been that the demonstration of a non-correlation would permit definite scientific conclusions. On the other hand, the finding of a positive correlation would leave us, from the standpoint of logic, very nearly where we were before. That is, the possibility that nicotine (or some other smoke ingredient) may contribute to the atherosclerotic process would remain open, but the existence of a correlation would not be sufficient to demonstrate that nicotine or other ingredient actually does so. The reason, of course, is that the subjects were not randomized before the imposition of nicotine dosage (or smoking) as would be the case in an animal experiment, but were self-selected. If smoking is a response to constitutional factors of temperament, personality, ability to cope with stress and anxiety etc. and is therefore associated with a whole "style of life" that is different from that of non-smokers, as many evidences seem to indicate, then these factors or life habits (exercize, sleep, use of aspirin, coffee drinking, alcohol consumption, diet etc.) might themselves be the causes of the differences in degree of arterial atherosclerosis and only be reflected in the smoking practises.

Your findings suggest that we may have to undertake still further controlled animal experiments, hopefully using better models and design than the previous ones, to isolate and evaluate any specific nicotine effect that may exist. They also suggest that we may need to extend further our studies of personality and "style of life" in smokers as compared to non-smokers. Still further, they suggest that we must continue and intensify our efforts to perfect biochemical methods of comparing the actual nicotine absorption by pipe, cigar and cigarette smokers under their habitual conditions of tobacco use.

I am afraid that when this paper is presented publicly, we may be called upon for comment, though we generally dislike to do so in the public press. If compelled to do so, the kinds of comments we would be inclined to make are implied in those outlined above. It would be quite unfortunate, I think, if there appeared to be any disparity between your views and ours on the interpretation or implications of these results. That there should be any actual disparity seems to me very unlikely, but reporters sometimes like to create the appearance of a controversy. This could probably be avoided if you see the implications as we see them and disarm the press by including in your presentation a caution against overinterpretation. Then, if we were forced to comment, we could simply emphasize our agreement with you.

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If you feel that this matter needs discussion I can probably arrange to stop off in New Orleans on my forthcoming trip to Texas.

Very sincerely yours,

RCH:tih
enclosure

Robert C. Hockett, Ph.D.
Associate Scientific Director

P.S. If full copies of the various papers you are presenting at the meeting could be made available to us in advance, it would be very helpful.